A FAMILY WITH OBSTRUCTIVE CARDIOMYOPATHY (ASYMMETRICAL HYPERTROPHY)

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In a recent paper, one of us (Teare, 1958) described 8 examples of a hitherto little recognized type of heart disease under the title *Asymmetrical hypertrophy of the heart in young adults*. The lesion was thought to be a benign tumour or hamartoma and was confined to the left ventricle, especially in the region of the septum. One of these patients, a woman of 21, had been under the care of Hammersmith Hospital, and by chance a sister was found to have heart disease when admitted there for routine tonsillectomy. Shortly afterwards an apparently healthy brother, aged 16, dropped dead when cycling to work. These findings led us to make a study of the entire family which is reported in this paper.

We were able to trace all members of the family for two generations, totalling 23 persons. In 14 of the 19 still alive we performed clinical, radiological, and electrocardiographic examinations. One man (Case 3) aged 47, apparently well, would not permit examination of himself or his four children (Cases 12 to 15). Full clinical details were available in two of the four who died, and the autopsy findings in three. We could obtain no information at all on the man (Case 1) who died in 1923, aged 18, possibly of meningitis (Table I).

As can be seen from the family tree (Fig. 1), we found evidence of heart disease in the three sibs

FIG. 1.—Family tree.

TABLE I
FINDINGS OF TWO COMPLETE GENERATIONS OF THE AFFECTED FAMILY

Case No.	Age	JVP	Second heart sound	Murmurs		c.t.r. and x-ray	Electro-cardiogram	Course
				Systolic	Diastolic			
1.	18	Died, 1923	No details	—	—	—	—	Died, ? meningitis
2.	40	+15	Wide split	Gr. 1 apical	0	60% RA LA LV+	Axis-20% Gross LBBB	Died, heart failure
3.	47	Examination refused						Apparently well
4.	40	+3	N	0	0	48% ? L.V.+	L.A.+	Alive
5.	37	N	N	0	0	56% RA LA RV LV+	LA+ LV+	Alive
6.	44	N	N	0	0	52%	TIH inv.	Alive
7.	21	+3	N	Gr. 1 apical	MDM	54% RA LA LV+	RA+ RBBB TIH inv.	Died suddenly
8.	18	Well till sudden death. No examination						Died suddenly
9.	14	N	Wide split	Gr. 2 at LSE	Early at LSE	47% LV+ RV+	Axis-70° TI inv.	Alive
10.	12	N	Wide split	Gr. 2 at LSE	MDM at LSE	56% RA LA RV LV+	Axis-30° RA+ LV+	Alive
11.	11	+5	Wide split	Gr. 2 at apex and LSE	Gr. 3 early at LSE	52% RA+ RV+ LA+	TIH inv.	Alive
12-15	Children of Case 3. Examination refused							Alive
16.	7	N	N	0	0	45%	TIH inv.	Alive
17.	7	N	N	0	0	51% LA+ LV+	TIH inv.	Alive
18.	7	+3	N	0	0	48% RA+ LA+	RA+	Alive
19.	4	+5	N	0	0	51% LV full	TIH inv.	Alive
20.	2	N	N	0	0	55% LV full	TIH inv.	Alive
21.	1	N	N	0	0	48%	TIH inv.	Alive
22.	15	N	N	0	0	—	—	Alive
23.	10	N	N	0	0	—	—	Alive

Murmurs and heart sounds graded 1-4.
L.S.E.=left sternal edge.
c.t.r.=cardiothoracic ratio.
MDM=mid-diastolic murmur.
JVP=Jugular venous pressure.

1st sound in Cases 2 and 6 split, otherwise normal.
Summation gallop in Cases, 2, 18, and 19.
3rd sound in Cases 5, 7, and 10.
4th (atrial) sound in Case 5.

of the brother and sister who had died suddenly (Cases 7 and 8), and also found that the father of these children had died of heart disease of a similar type. One of the brothers of this man had an abnormal heart as did at least two of the brother's five children. In all, 9 of the 23 persons had unequivocal evidence of heart disease and a further three had possible evidence.

A description will now be given of the clinical radiological, electrocardiographic, and pathological findings in the nine affected members of this family.

CLINICAL FINDINGS

Age and Sex. The three fatal cases died at 18, 21, and 40, while the ages of the living patients range from 4 to 37 years. The disease seems more severe at an earlier age in the latest generation affected. Of the nine affected patients, four are male and five are female.

Symptoms. Of the living patients Case 5, aged 38, has had exertional dyspnoea for five years, chest pain on walking for three years, and recently hæmoptysis after sexual intercourse. Case 13, aged 12, and Case 18, aged 7, both have slight dyspnoea on exertion and Case 13 in addition suffers from abdominal pain.

Of the patients who have died, Case 2, aged 40, who was the father of Cases 7 to 11, was found to have an enlarged heart at the age of 35: he had chest pain when 39 but was reasonably well until a month before death when he suddenly developed congestive heart failure. Case 8 died suddenly while riding to work on a bicycle at the age of 18: he had previously been perfectly well. Case 7, aged 21 (Case 5 of Teare, 1958), was said to have had rheumatic fever at the ages of 8 and 12 years but there was subsequently no evidence of this, and a diagnosis of congenital heart disease was made. At the age of 19 abdominal pain led to a fruitless laparotomy, and soon afterwards she had a cerebral embolus following the development of atrial fibrillation. At the age of 21 when running for a bus she collapsed and died.

Signs. Only one patient (Case 2) had been in severe congestive heart failure, with ascites and a jugular venous pressure 15 cm. above the sternal angle. In two others (Cases 11 and 19) the jugular venous pressure was +5 cm. with *a* and *v* waves of equal heights. In a further five the *a* wave was prominent but not abnormally so.

The *arterial pulse* and blood pressure were normal in all patients except Case 7 who developed atrial fibrillation two years prior to death. The *cardiac impulses* were impalpable in two, a tapping apex beat with parasternal lift was found in five, and a left ventricular apex beat in one.

The first sound was normal in all except one patient (Case 2) in whom it was split and there was left bundle-branch block. The second sound also was abnormally widely split in this man and in his three living children (Cases 9 to 11) (Fig. 2), none of whom had bundle-branch block. It was normal in the remainder. A third sound was heard in three patients and may be presumed to be abnormal in Case 5 at the age of 37. One patient had a clear atrial (fourth) sound (Fig. 2) and a further three had a summation gallop. Thus, extra sounds were common in these patients.

Systolic murmurs were present in five. In four of these there was also a *diastolic murmur*—in Case 7 an apical mid-diastolic murmur, but in the other three an early or delayed murmur, maximal at the left sternal edge. In Case 10 the murmur was louder with inspiration, was scratchy in quality, and closely resembled that found in Ebstein's disease (Fig. 3).

All the patients tended to be of a short stocky build. No other congenital anomalies were noted. One patient (Case 5) had severe iritis and mild arthritis.

Electrocardiography. The abnormal leads of the cardiograms of Cases 2 and 5 and of all their sibs (except Case 8) are shown in Fig. 4 and 5. A right atrial P wave was found in five and was considerable in two (Case 9 and 10). Left bundle-branch block occurred in Case 2. An S wave greater than R in V5 was seen in three. The electrical axis was abnormal in three being -20° , -30° , and -70° . In all cases except the three with left axis deviation there was a striking similarity in lead III which showed a sharply inverted T wave usually preceded by a Q wave. Similar changes were seen in aVF although in four cases the T inversion was present only in lead III. The cause of the abnormality is not clear but presumably it is derived from muscle in or near the hypertrophy

in the septum. In hearts that are electrically in a vertical or intermediate position the potentials in the antero-septal or postero-septal region could well be directed chiefly to leads aVF and III. The left præcordial leads or equivalents (V5, V7, aVL, and I) were abnormal in six cases showing a low

FIG. 2.—Phonocardiogram of Case 9, showing atrial sound and widely split second sound.

FIG. 3.—Phonocardiogram of Case 10, showing increase in diastolic murmur on inspiration and widely split fixed second sound.

voltage or inverted T wave. The præcordial QRS voltage was abnormal in two, both showing left ventricular preponderance.

Radiology. The overall heart size was increased in seven of the nine affected cases, cardio-thoracic ratios 47–60 per cent. Individual chamber enlargement was found as follows: right atrium in 6, left atrium in 7, and left ventricle in 5 cases. The aorta was noticeably small in six cases.

The cardiac silhouette in the postero-anterior projection was somewhat globular in all (Fig. 6 and 7). This appearance was mainly due to prominence of the right atrium and a straight or slightly curved left border.

Genetics. The condition is a dominant one, not sex-linked. The apparent slight excess of affected subjects on the basis of a 1:1 ratio among children of affected parents is not greater than might occur by chance.

FIG. 4.—Leads I, II, III, aVF, V1, and V5 of the electrocardiograms from Case 2 and his offspring (Cases 7, 9, 10, and 11).

FIG. 5.—Leads I, II, III, aVF, V1, and V5 from Case 5 and his offspring (Cases 17 to 21).

FIG. 6.—Diagrams of the postero-anterior cardiac silhouette of Cases 2, 5, 7, 9, 10, 11, 17, 18, 19, 20, and 21, with their cardiothoracic ratios.

FIG. 7.—Six foot postero-anterior chest film of Case 7, showing globular heart and enlargement of both atria.

FIG. 8.—The heart of Case 8, opened from the front to show the massive hypertrophy of the septum and anterior wall of the left ventricle.

Pathology. This has been dealt with at length in a previous paper (Teare, 1958) but we are reporting here a fuller account of Case 8 who was mentioned there only in an addendum, and also a description of Case 2. Case 7 of this series is Case 5 in Teare's paper.

Case 8. The heart weighed 425 g. and showed well-marked hypertrophy which was localized to the septum and to the anterior wall of the left ventricle (Fig. 8). The mass of muscle forced the septum over into the right ventricle. Histological examination revealed large coarse muscle bundles with large clefts between them and scattered fibrosis (Fig. 9). The appearances were thus closely similar to those of Case 7 and to those reported previously (Teare, 1958).

Case 2. The heart weighed 530 g. and the left ventricle was slightly hypertrophied with recent antemortem thrombus attached to the apical part of the septal wall. There was well-marked fibrotic scarring of the distal three quarters of the interventricular septum, which microscopically showed gross and coarse fibrous replacement.

Cases 6, 17, and 20 were all *doubtful cases*, since all were normal on clinical examination but had slight cardiac enlargement on X-ray (Fig. 6) and T wave inversion in lead III of the electrocardiogram, which might have been positional in nature since VF was normal (Fig. 5).

DISCUSSION

One of the striking features of asymmetrical hypertrophy is the very close similarity of all the hearts that have been examined pathologically (Teare, 1958). The familial incidence indicates that it is an inherited disorder. No other congenital defects or biochemical or neurological lesions are associated. The clinical picture, while not as nearly identical in each patient as the pathological appearances, has a certain uniformity. The diffuse cardiac impulse, gallop rhythm, systolic and

FIG. 9.—Photomicrographs of the heart muscle in Case 8. Hæmatoxylin and eosin.

(A) Showing large muscle bundle and coarse fibrosis, with separation. $\times 25$.

(B) Showing scattered fibrosis. $\times 110$.

delayed rough diastolic murmurs, right atrial prominence with a globular cardiac silhouette radiologically, and right atrial P waves are all reminiscent of Ebstein's disorder of the tricuspid valve. While there is no anatomical similarity, some functional parallel might be drawn between the two conditions, for in both obstruction to right ventricular inflow is present, as shown by the increase with inspiration of the intensity of the diastolic murmur in Case 10. Presumably the clinical picture and course of the disorder depends upon the site of maximum obstruction produced by the asymmetrical hypertrophy. One patient in the series described by Teare (1958) presented with signs of obstruction to the mitral valve due to the mass of muscle blocking and distorting the valve from the ventricular aspect. We have also seen a similar though not necessarily identical condition obstructing the outflow of the left ventricle and simulating aortic stenosis (Goodwin *et al.*, 1960).

It is clear, therefore, that the manifestations of asymmetrical hypertrophy are protean, although in the families reported here, obstruction to valves other than possibly the tricuspid was not found. However, we believe that the disease merits the general title of obstructive cardiomyopathy, and should be thought of when signs of valvular obstruction with atypical features are found in a subject with a familial history of heart disease.

The condition does not appear to have been described prior to the paper by Teare (1958). It does not resemble the cases of familial heart disease reported by Evans (1949) or by Campbell and Turner-Warwick (1956) in that the hypertrophy is asymmetrical, not generalized. Davies (1952) reported a familial heart disease involving five of nine siblings and one of their children, with some features of sub-aortic stenosis, and a tendency to sudden death. However, it is probable that asymmetrical hypertrophy is not unduly rare, for cases may masquerade under differing diagnoses, only coming to light at autopsy or because symptoms of severe cardiac obstruction demand surgical relief.

The prognosis appears to be very variable and, though uncertain, is not necessarily grave. Death may be expected to occur in one of five ways—suddenly from ventricular fibrillation, possibly connected with the extensive fibrosis scattered through the muscle bundles (Case 5 of Teare, 1958); from heart failure due to myocardial insufficiency; from heart failure from inflow or outflow tract obstruction; from embolism; or from injudicious cardiac surgery.

Eight of Teare's (1958) series of nine patients, which includes two in this series (7 and 8), died

suddenly, three having had previous symptoms of palpitation, dizziness, or syncope, and one congestive heart failure. Another had suffered a cerebral embolism during an episode of atrial fibrillation. Yet another had attacks of pulmonary oedema, signs of mitral obstruction, and died following mitral valvotomy (Case 4 of Teare, 1958).

In the present series most patients are under the age of 16, but four are between the ages of 30 to 50 years. No real estimate can be made of the prognosis from the available data in view of the many variable factors and the purely autopsy character of the series described by Teare (1958).

Correct diagnosis depends upon awareness of the possibility of the condition, which should be suspected if there is a family history of heart disease and if the clinical picture suggests a mild form of tricuspid stenosis or of Ebstein's syndrome without bundle-branch block. The cardiogram is likely to help in this respect for we have seen only one case with right bundle-branch block, whereas this is almost invariable in Ebstein's syndrome. The finding of a deeply inverted T wave preceded by a Q wave in leads III and VF may be of some value in diagnosis.

In view of the tendency to arrhythmia and sudden death we have not employed investigations such as cardiac catheterization and angiocardiography. We do not know whether surgery would have anything to offer in this group, although surgical treatment has been successfully carried out in one patient with sub-aortic obstruction due to obstructive cardiomyopathy (Goodwin *et al.*, 1960). If symptoms demand relief and signs suggest notable valvular obstruction, then cardiac catheterization and angiocardiography will be justified to confirm the diagnosis and to assess the feasibility of surgical relief. We have employed both these investigations in the aortic type of obstructive cardiomyopathy without any ill effects to the patients (Goodwin *et al.*, 1960). But surgical exploration may still be necessary in some cases (Teare, 1958). In general, however, treatment should be conservative and directed towards preventing and controlling arrhythmias and congestive heart failure.

SUMMARY

A family with a disorder of heart muscle (asymmetrical hypertrophy) of inherited nature, notable for sudden death, and with clinical features suggesting obstruction to the inflow tract of the right ventricle, is described. The clinical aspects and manifestations, diagnosis, prognosis, and pathology are described, and the title of *obstructive cardiomyopathy* is proposed for these and similar cases.

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